REMARKS

Claims 3, 4, 7, 8, 18, 31 and 33-37 are pending in the subject application. Claims 33 - 37 have been withdrawn by the Examiner. Applicants have amended claim 18. The amendment to the claim 18 does not involve any issue of new matter and therefore applicants request the amendment be entered. Upon entry of this Amendment the claims pending and under examination will be claims 3, 4, 7, 8, 18, 31, as amended.

Priority

On page 3 of the April 15, 2010 Office Action the Examiner indicated that the specification should contain the priority data because "This application is 371 of PCT/FR99/02588 (10/25/1999)".

With respect, applicants note that this application is not a §371 national stage application. Although the application was originally filed as a §371 application the status of the subject application was changed to a §111 application as indicated in the December 7, 2004 Decision in response to applicants' Petition Under 37 C.F.R. §1.182, filed July 20, 2004.

Accordingly, applicants request that the Examiner reconsider and withdraw this ground of objection.

Information Disclosure Statement; Copending Application

The Examiner indicated that the Information Disclosure Statement filed December 7, 2009 contains a large number of references. The Examiner requested that applicants point out the most relevant references. The Examiner further indicated that the listing of references in the specification is not a proper Information Disclosure Statement.

In response, applicants note that there is no requirement that applicants point out the most relevant references to the Examiner. Applicants are required to disclose all information which an Examiner might consider material in deciding whether to allow an application and therefore must disclose references which they think are not material or even relevant if it could later be asserted that an Examiner could have considered the reference material. Accordingly, applicants respectfully request that the Examiner review the Information Disclosure Statement filed December 7, 2009, consider the references, and make the references of recorded by initialing the Forms PTO 1449 (substitute) which we included with the December 7, 2009 Information Disclosure Statement. In addition, applicants note that the references listed in the subject specification have been included in the Information Disclosure Statement filed December 7, 2009.

Copending applications

The Examiner indicated on page 4 of the April 15, 2010 Office Action that applicants must bring to the attention of the Examiner information within their knowledge as to other copending U.S. applications which are "material to patentability" of the application in question.

As an initial matter, applicants' understand that the Examiner is already aware of U.S. Patent No. 6,831,073 issued December 14, 2004 on behalf of Michael Lanquetin. This patent was disclosed in the Information Disclosure Statement filed September 17, 2007. On page 7-8 of the April 15, 2010 Office Action the Examiner has rejected claims 3, 4, 7, 8, 18 and 31 on the ground of obviousness-type double patenting over claims 1-6 of U.S. Patent 6,831,073.

Other Copending applications

In order to insure compliance with the duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following copending applications or patents, the claimed subject matter of each of which concerns methods of contraception, not methods of hormonal replacement therapy.

1. U.S. Serial No. 11/649,672, filed January 3, 2007, was disclosed in an Information Disclosure Statement filed September 17, 2007. This application was published as US 2007-0281912 A1 on December 6, 2007 and this publication number was disclosed in an Information Disclosure Statement filed December 4, 2009. On July 10, 2010 U.S. Serial No. 11/649,672 issued as U.S. Patent No. 7,749,987 B2 and applicants direct the Examiner's attention to item 1 of the Supplemental Information Disclosure Statement that begins on page 12 of this paper.

2. U.S. Serial No. 12/079,335, filed March 25, 2008 was published as US 2008-0242650 A1 on October 2, 2008. This patent application publication number is listed as item 2 of the Supplemental Information Disclosure Statement that begins on page 12 of this paper.

3. U.S. Patent No. 6,906,049, issued June 14, 2005 in the name of Paris et al. was disclosed in the Information Disclosure Statement filed September 17, 2007.

Specification

The Examiner indicated on page 4 of the April 15, 2010 Office Action

that the specification has not been checked to the extent necessary to determine the presence of all possible minor errors. The Examiner requested applicants' cooperation in correcting any errors of which applicants may become aware. At the present applicants are not aware of any errors requiring correction.

Rejections Under 35 U.S.C. §112

The Examiner rejected claims 18 and 3, 4, 7, 9 and 31 under 35 U.S.C. §112, first paragraph, as failing to comply with the Written Description requirement. The Examiner asserted that the claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner asserted that claim 18, which is drawn to "a method of treating menopause women" is not limited to a particular method and covers the method for any treatment. The Examiner further asserted that the details of "continuous without interruption" is not described in the specification. The Examiner indicated that it is unclear how oral administration can be continuously uninterrupted unless given by infusion.

In response, applicants respectfully traverse the Examiner's ground of rejection. Nevertheless, without conceding the correctness of the Examiner's rejection, claim 18 has been amended hereinabove.

Amended claim 18 provides a hormonal replacement therapy method for treating an estrogen deficient, menopausal woman comprising orally administering daily without interruption to such menopausal woman a composition containing from 0.5 to 1.5 mg of free estradiol or 1.5 to 2 mg of an estradiol ester, and from 0.625 to 1.25 mg of nomegestrol acetate per daily dose so as to induce and maintain endometrium

atrophy without bleeding.

The specification discloses on page 1 that the pharmaceutical compositions disclosed therein are designed to correct estrogen deficiencies in women, regardless of their origin, and more particularly in menopausal women. The specification further discloses on page 11 that the mode of combined administration is indicated in menopausal women, whether the menopause is natural or the result of surgery; the estrogen-progestative combination is intended to compensate for the functional disturbances induced by the menopausal estrogen deficiency, while maintaining endometrial atrophy and avoiding the appearance of deprivation bleeding in most women. Moreover, the specification discloses on page 21 treatment for 6 consecutive months of 179 women who had been menopausal for at least 3 years, with 1.5 mg per day of estradiol combined continuously with 4 different doses of nomegestrol acetate. As discloses on page 22 of the specification, the results show that low doses of nomegestrol acetate administered in continuous combination with an estrogen are capable of preventing growth of the uterine mucosa and keeping it in an atrophic condition, whereas in contrast higher doses, they are insufficient to induce a secretory transformation of the endometrium.

With regard to the Examiner's comment regarding the recitation of "continuous without interruption", applicants note that amended claim 18 no longer recites "continuous without interruption" but instead recites "comprising orally administering daily without interruption".

Thus, applicants maintain that the specification satisfies the written description requirement for amended claim 18 and the claims dependent therefrom. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection under 35 U.S.C. §112, first paragraph

Double Patenting Rejection

On pages 7-8 of the April 15, 2010 Office Action the Examiner rejected claims 3, 4, 7, 8, 18 and 31 on the ground of obviousness-type double patenting over claims 1-6 of U.S. Patent 6,831,073. The Examiner indicated on page 23 of the April 15, 2010 Office Action that this double patenting rejection is maintained because the invention is inherently taught by the reference. Specifically, the Examiner asserted that the combination and dosage overlap and therefore the property adherent to the amount and dosage of the components are considered inherent.

In response, applicants respectfully traverse the Examiner's ground of rejection. Nevertheless, without conceding the correctness of the Examiner's rejection, applicants will consider submitting a terminal disclaimer once otherwise patentable subject matter has been indicated.

Rejections Under 35 U.S.C. §103

Applicants' claimed invention provides the following:

Claim 18: A hormonal replacement therapy method for treating an estrogen deficient, menopausal woman comprising orally administering daily without interruption to such menopausal woman a composition containing 0.5 to 1.5 mg of free estradiol or 1.5 to 2 mg of an estradiol ester, and from 0.625 to 1.25 mg of nomegestrol acetate per daily dose so as to induce and maintain endometrium atrophy without bleeding. [Emphasis added]

Claim 31: A pharmaceutical composition in oral administrable form comprising, in combination, from 0.5 to 1.5 mg of

> free estradiol or 1.5 to 3 mg of an esterified estradiol and from 0.625 to 1.25 mg of nomegestrol acetate. [Emphasis added]

Applicants' claimed invention is based on the surprising and unexpected discovery that a daily dose of 0.625 to 1.25 mg nomegestrol acetate can be used, in combination with 0.5 to 1.5 mg of free estradiol or 1.5 to 2 mg estradiol ester, as hormone replacement therapy to treat an estrogen deficient menopausal woman so as to induce endometrium atrophy, i.e. to prevent growth of uterine mucosa, without inducing bleeding.

Applicants' claimed invention is further based on the surprising and unexpected discovery that when a daily dose of 0.625 to 1.25 mg nomegestrol acetate is administered, in combination with specific amounts of free estradiol or estradiol acetate, the anti-estrogenic effect of nomegestrol acetate can be decoupled from the progestational effect.

1. Rejection Under 35 U.S.C. §103 over Jamin in view of Martindale, Bazin et al., Paris et al. and Hodgen

As noted above, applicants' claimed invention relates to hormone replacement therapy for estrogen deficient menopausal woman. This method is achieved by administering daily without interruption a composition containing from 0.5 to 1.5mg of free estradiol or 1.5 to 2mg of an estradiol ester, and from 0.625 to 1.25mg of nomegestrol acetate per daily dose so as to induce and maintain endometrium atrophy without bleeding.

Thus, applicants' claimed invention is unrelated to contraception for a woman undergoing a normal menstrual cycle, i.e. a woman who is not menopausal.

Therefore, applicants maintain that they do not understand the relevance of the cited references which concern contraception in non-menopausal women and are confused by the Examiner's discussion of the obviousness of using applicants' claimed dosage regimen for contraception. Clearly, there is no motivation to use a contraception regimen for hormone replacement therapy for estrogen deficient menopausal woman.

Moreover, none of the references cited in this ground of rejection disclose applicants' claimed dosage of 0.625 to 1.25 mg of nomegestrol acetate. Furthermore, applicants' claimed dosage is neither contained within, nor overlaps with, the dosage of nomegestrol acetate disclosed in the cited references. Accordingly, applicants maintain that there is no basis for a prima facie case of obviousness.

Finally, as noted above, applicants' claimed invention provides unexpected advantages and results which could not have been predicted from the cited references.

In view of the preceding remarks applicants request that the Examiner reconsider and withdraw the rejection of claims 3, 4, 7, 8, 18 and 31 over Jamin in view of Martindale, Bazin et al., Paris et al., and Hodgen.

2. Rejection Under 35 U.S.C. §103 Over Plunkett et al. and Blanc et al.

As acknowledged by the Examiner, Plunkett et al. do not disclose use of nomegestrol acetate at all, let alone use of 0.625 to 1.25 mg nomegestrol acetate per daily dose.

Blanc et al. disclose use of a dose of nomegestrol of 2.5 mg/day, not

the 0.625 to 1.25 mg range presently claimed. (Applicants note that the Examiner has incorrectly stated on page 21 of the April 15, 2010 Office Action that a lower limit of 0.3 mg nomegestrol acetate is presently claimed.)

Blanc et al. further disclose an estradiol dose of 2mg versus the currently claimed dose of 0.5 to 1.5mg of free estradiol. (Applicants note that the Examiner has incorrectly stated on page 21 of the April 15, 2010 Office Action that 0.3 to 3mg of estradiol is claimed).

Thus, applicants' claimed method involves a dose range of nomegestrol acetate and a dose range of free estradiol, neither of which dose ranges are included within, or overlap with, the ranges disclosed in the cited references. Accordingly, there is not a prima facie case of obviousness.

Moreover, as noted above, applicants' claimed invention provides unexpected advantages and results which could not have been predicted from the cited references.

In view of the preceding remarks applicants request that the Examiner reconsider and withdraw the rejection of claims 3, 4, 7, 8, 18 and 31 over Plunkett et al. and Blanc et al.